

**In the Claims**

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Please amend page 21, line 1 as follows:

[C L A I M S]

**What is claimed is:**

Please amend claim 4 as follows:

- a
4. (once amended) The method of [any of claims 1 to 3] claim 1, wherein the assay reagent is a compound which contains an artificially <sup>v2, 2nd</sup> high concentration of an NMR active nucleus.

Please amend claim 6 as follows:

- a<sup>2</sup>
6. (once amended) The method of [any of claims 1 to 5] claim 1, wherein the assay reagent is an organic compound comprising one or more NMR active nuclei associated with a bond which is broken during the course of the assay.

Please amend claim 8 as follows:

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A<sup>3</sup>

8. (once amended) The method of [any claim 1-7]claim 1, wherein the assay reagent is analysed repeatedly in step c) at known time intervals so as to generate information about a change with time of the assay reagent.
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Please amend claim 9 as follows:

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A<sup>4</sup>

9. (once amended) The method of [any one claim 1 to 8]claim 1, wherein the [asseay]assay reagent is a Nucleotide, or nucleotide analogue, polynucleotide, amino acid analogue, polypeptide or protein.
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Please amend claim 10 as follows:

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A<sup>5</sup>

10. (once amended) The method of [any one of claims 1 to 9]claim 1, wherein the assay is a nucleic acid hybridisation assay.
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Please amend claim 11 as follows:

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A<sup>6</sup>

11. (once amended) The method of [any one of claims 1 to 10]claim 1, wherein the assay is a binding assay.
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Please amend claim 12 as follows:

- A<sup>7</sup>
12. (once amended) The method of [claims 1 to 11]claim 1, wherein the assay reagent is a compound specifically labelled with at least one NMR active nucleus and the assay reagent is administered to a micro-organism, macro-organism or cultured cells, cellular metabolites or an excretion product of the assay reagent are hyperpolarised and analysed by nuclear magnetic resonance spectroscopy, nuclear magnetic resonance imaging or both.

Please amend claim 13 as follows:

- A<sup>8</sup>
13. (once amended) The method of [claims 1 to 12]claim 1, wherein the assay is a binding study performed using micro-organisms or cultured cells

Please amend claim 14 as follows:

- A<sup>9</sup>
14. (once amended) The method of [claims 1 to 13]claim 1 wherein the hyperpolarisation transfer is repeated to enhance the signal-to-noise ratio.

Please amend claim 15 as follows:

- A<sup>10</sup>
15. (once amended) The method of [claim 1 to 14]claim 1 wherein the shortening

a<sup>10</sup>  
cont

effect as expressed by the improvement of signal-to-noise per unit time is a factor of 10 or more compared to known assay techniques without hyperpolarisation.

Please amend claim 16 as follows:

a<sup>11</sup>

16. (once amended) The method of [claims 1 to 15]claim 1 where the hyperpolarisation of the NMR active nucleus of the assay reagent is carried out by polarisation transfer from a hyperpolarised noble gas, or a mixture of hyperpolarised noble gases.

Please amend claim 19 as follows:

a<sup>12</sup>

19. (once amended) The method of [claims 16 to 18]claim 16 wherein the hyperpolarisation is transferred by a hyperpolarised noble gas in solution and wherein the viscosity of the solution is at least 1000 mPs.

Please amend claim 20 as follows:

a<sup>13</sup>

20. (once amended) The method of [claims 1 to 15]claim 1 where the hyperpolarisation of the NMR active nucleus of the assay reagent is carried out by polarisation transfer at a temperature of 4.2 K or less in the presence of a magnetic field of at least 1 T.

Please amend claim 21 as follows:

- a<sup>14</sup>
21. (once amended) The method of [claims 1 to 15]claim 1 where the hyperpolarisation of the NMR active nucleus of the assay reagent is carried out by polarisation transfer using dynamic nuclear polarisation.

Please amend claim 22 as follows:

- a<sup>15</sup>
22. (once amended) The method of [claims 1 to 15]claim 1 where the hyperpolarisation of the NMR active nucleus of the assay reagent is carried out by para hydrogen induced polarisation.

Please amend claim 23 as follows:

- a<sup>16</sup>
23. (once amended) The method of [claims 1 to 15]claim 1 where the hyperpolarisation of the NMR active nucleus of the assay reagent is carried out with the spin refrigeration technique.

Please amend claim 24 as follows:

- a<sup>17</sup>
24. (once amended) The method of [claims 1 to 23]claim 1, wherein more than one

A<sup>17</sup>  
cont

assay is multiplexed and monitored by NMR spectroscopy and/or NMR imaging.

A<sup>18</sup>

Please amend claim 25 as follows:

25. (once amended) The method of [claims 1 to 24]claim 1 wherein the assay is performed in a multiwell or multispot assay array.

Please amend claim 26 as follows:

A<sup>19</sup>

26. (once amended) The method of [claims 1 to 25]claim 1 wherein step c) is performed by examining the assay reagent using both NMR spectroscopy to obtain more than one spectrum, and magnetic resonance imaging to obtain one or more discrete spectral location, and repeating the examination at least once so as to obtain quantitative information about kinetic or time-dependant alteration in chemistry, environment or structure of the assay reagent.

Please amend claim 27 as follows:

A<sup>20</sup>

27. (once amended) The method of [claim 1 to 26]claim 1, wherein step c) is performed in an aerosol or flow-through device applied to aerosol droplets where the well, surface or container is used to contain the assay reagent.

Please amend claim 28 as follows:

A 28  
cont

28. (once amended) An *in vitro* assay kit for carrying out the assay method as defined in claim 1 [to 27 ]which comprises: one or more assay reagents each containing at least one NMR active nucleus contained in a well or vial or other suitable container for carrying out the hyperpolarisation of step (b) of claim 1.

Please amend claim 29 as follows:

- A 29  
cont
29. (once amended) The *in vitro* kit of claim 28 where the NMR analysis of step (c) [of claim 1] is carried out in the same well, vial or container as the hyperpolarisation transfer is carried out.

**Remarks**

Claims 1-29 are pending in the instant application. Applicants have amended claims 4, 6, 8, 9, 10, 11, 12, 13, 14, 15, 16, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, and 29 to more fully conform with U.S. practice and to delete multiple dependencies. A version of the claims marked up to show the amendments, as well as a clean version of the claims encompassing the amendments, is attached hereto.